



Glycoscience
for
Better Health

バイオ医薬品開発のための ソリューション

株式会社糖鎖工学研究所
GlyTech, Inc.

2022 October

GlyTech, Inc.

Established: April 2, 2012 (**10th anniversary**)

Spun out from Otsuka Group

President & CEO: Mr. Hiroaki Asai

Head office: Kyoto

Website: www.glytech-inc.com

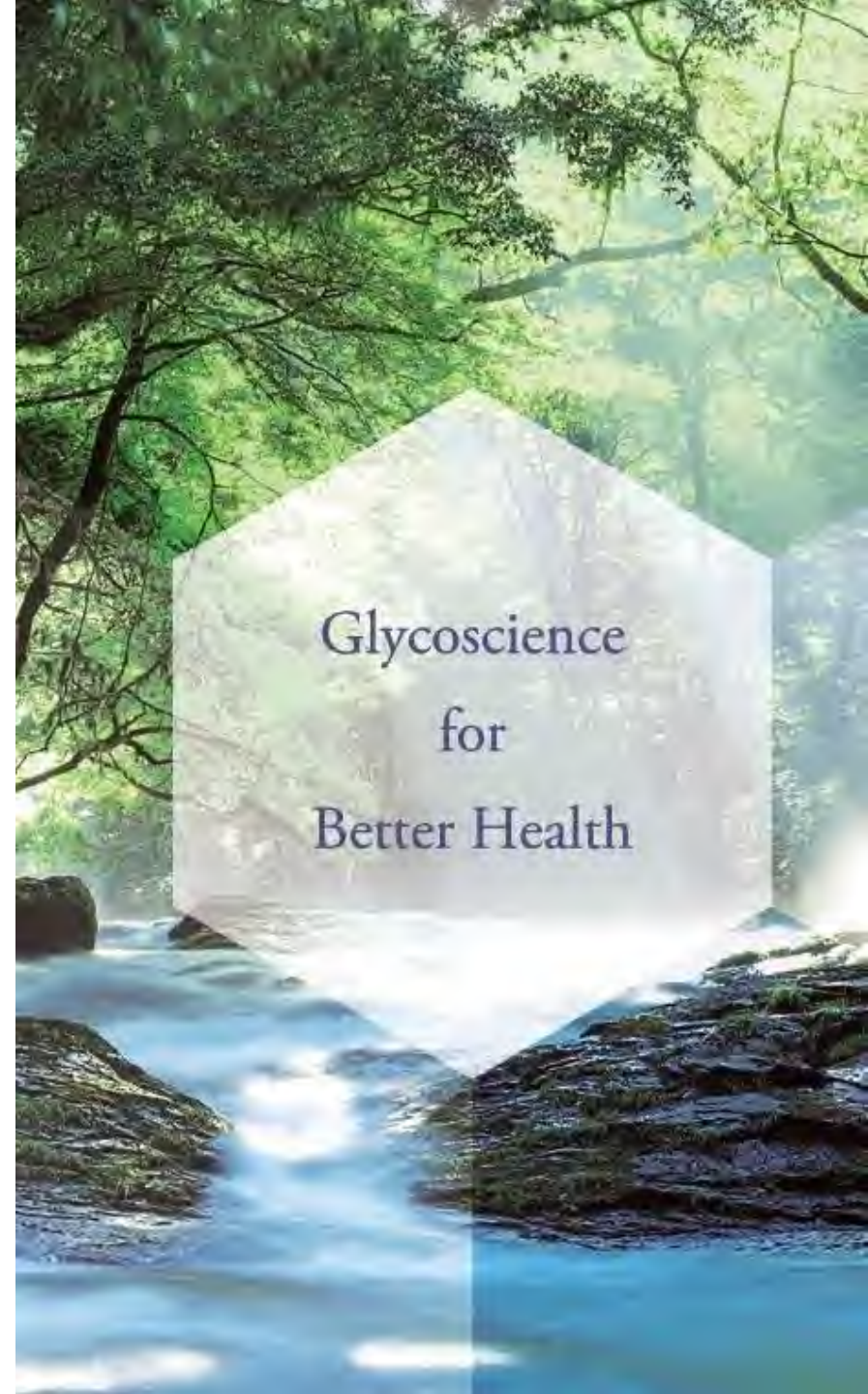


Vision

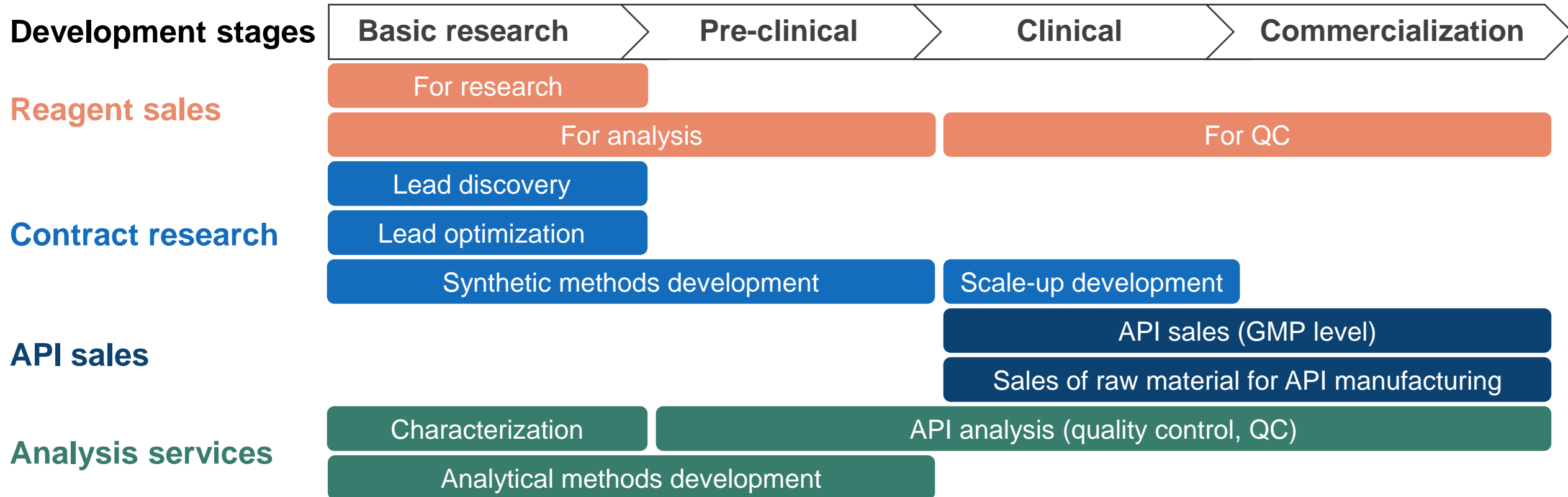
*Help to build a healthier world by creating new biotherapeutics and modalities with the aim of “**harmonizing with nature.**”*

Mission

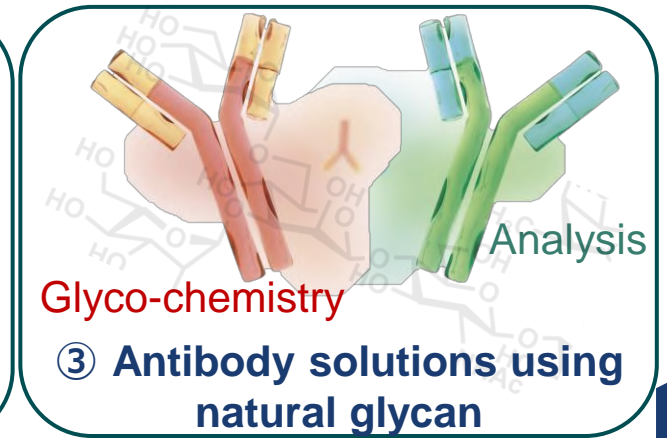
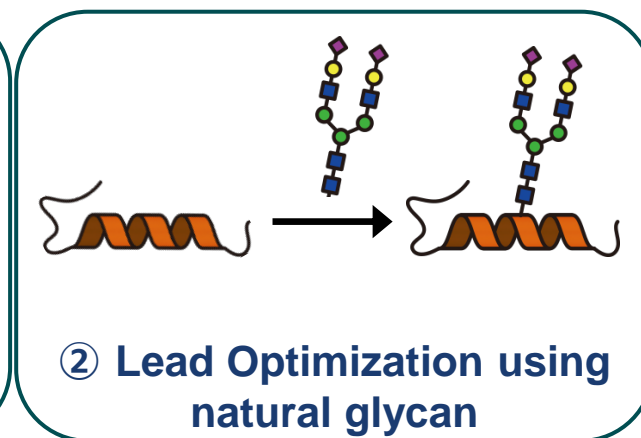
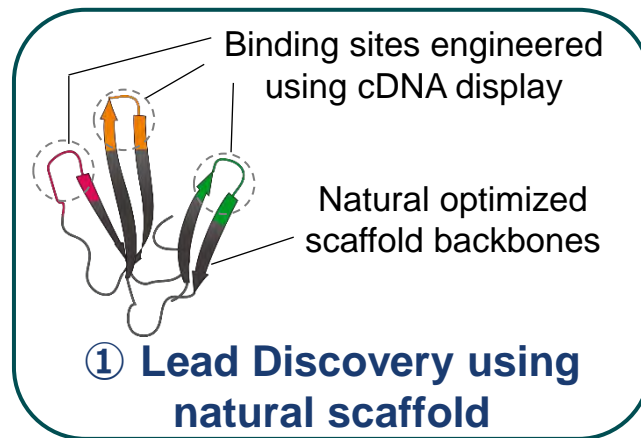
- *Develop innovative, versatile platform technologies using natural structures to realize new value*
- *Accelerate the development of new biotherapeutics and the improvement of existing biotherapeutics*

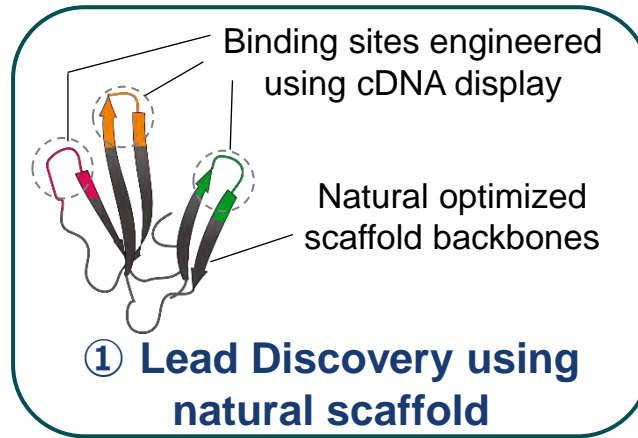


Business model and services



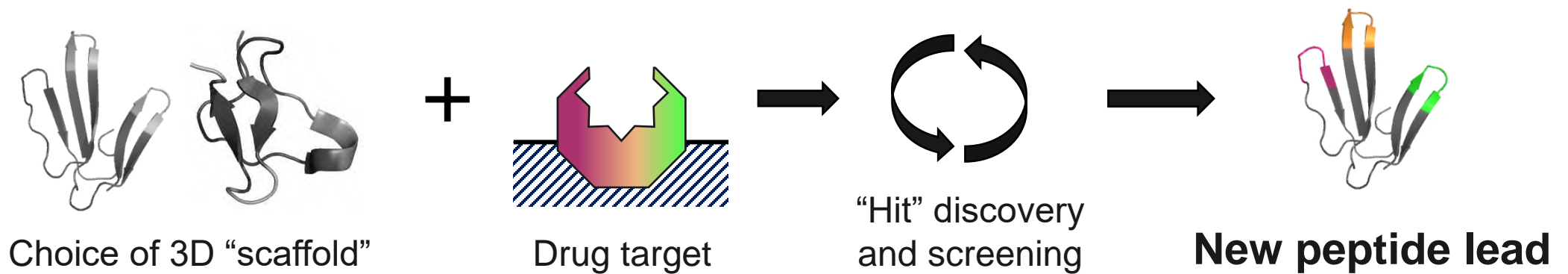
Core technologies and solutions





Lead discovery using natural scaffolds

Peptide Discovery Platform



Discovery platform: In vitro evolution

Strong leads

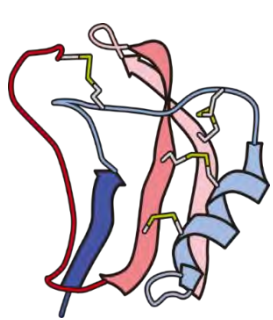
> 6 Evolutionarily optimized backbones (DRPs)

Disulfide-rich, 3D: Bioactive structure

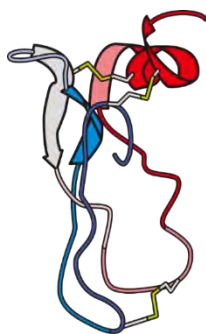
Low antigenicity: Avoid presentation to the MHC.

Protease resistance: Ideal stability

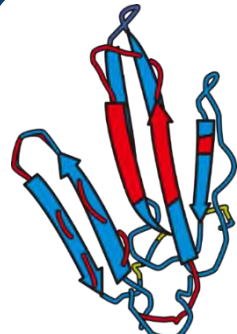
Multiple functionalities: Agonist/Antagonist



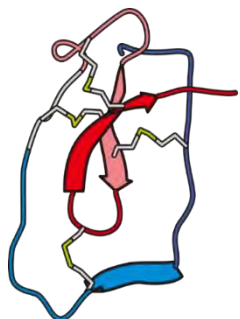
1 alpha, 3 beta



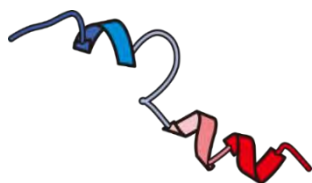
1 coil, 2 beta



4-5 beta



3 beta

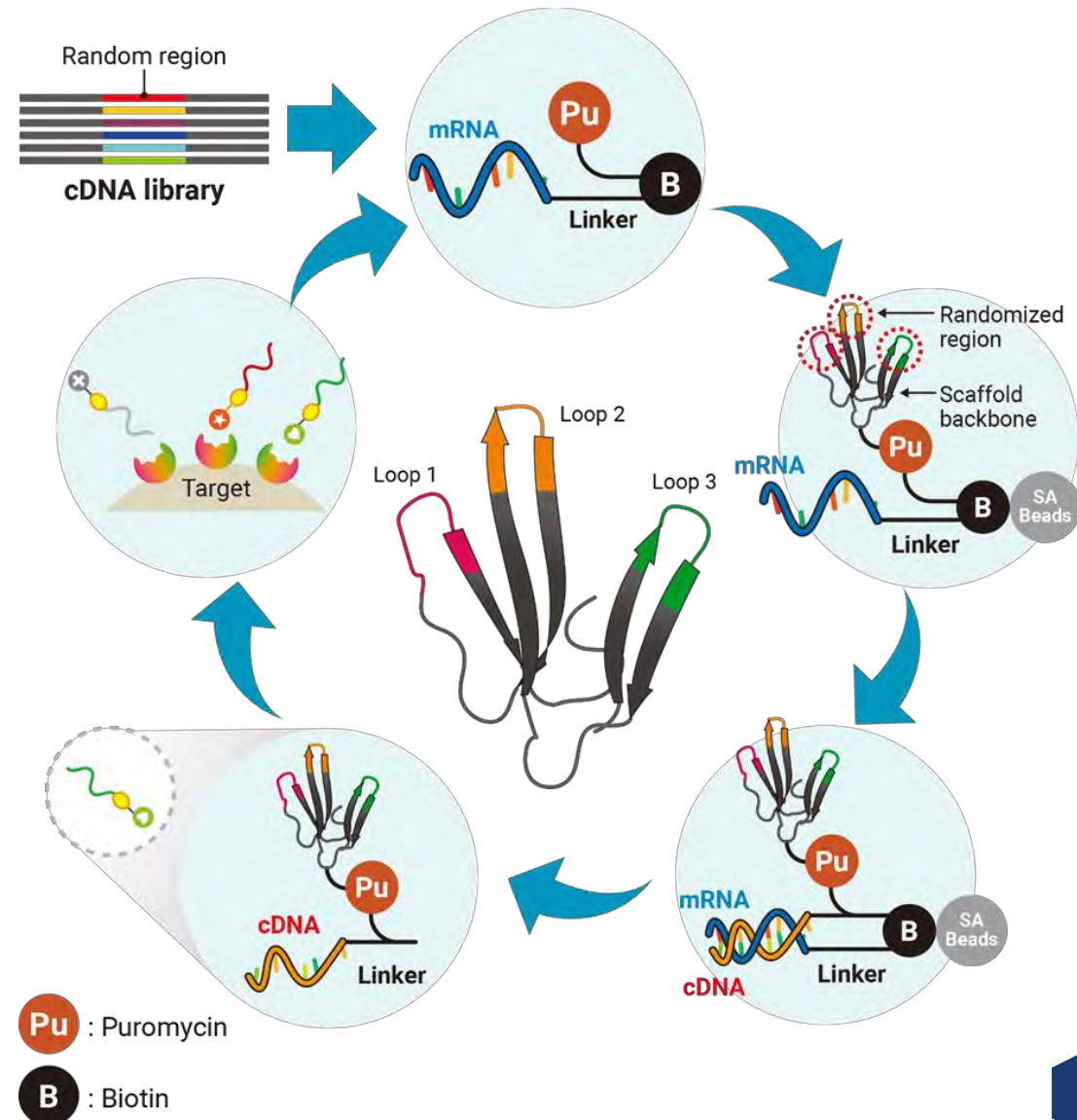


2 alpha
(1 alpha, 1 coil)



3 beta

Scaffold protein-based screening platform using cDNA display



Discovery platform: In vitro evolution

Highly efficient screening

100 times larger screening space (10^{11} – 10^{13})

6 times faster / cycle

10 times higher final fusion yield

(Compared with traditional mRNA display systems)

Seed compounds **against VEGF** discovered after 10 rounds of screening:

No.	Loop 1	Loop 2	Loop 3	Kd (nM)
1	PLTRVV	HGDHHTLSEW	EEPTAHV	2.1 ± 0.5
2	WEVLL	AHSVTLAHGH	TGPGAER	35 ± 5
3	TLWLSY	DVPQSGTNLA	ELTHPVD	14 ± 2

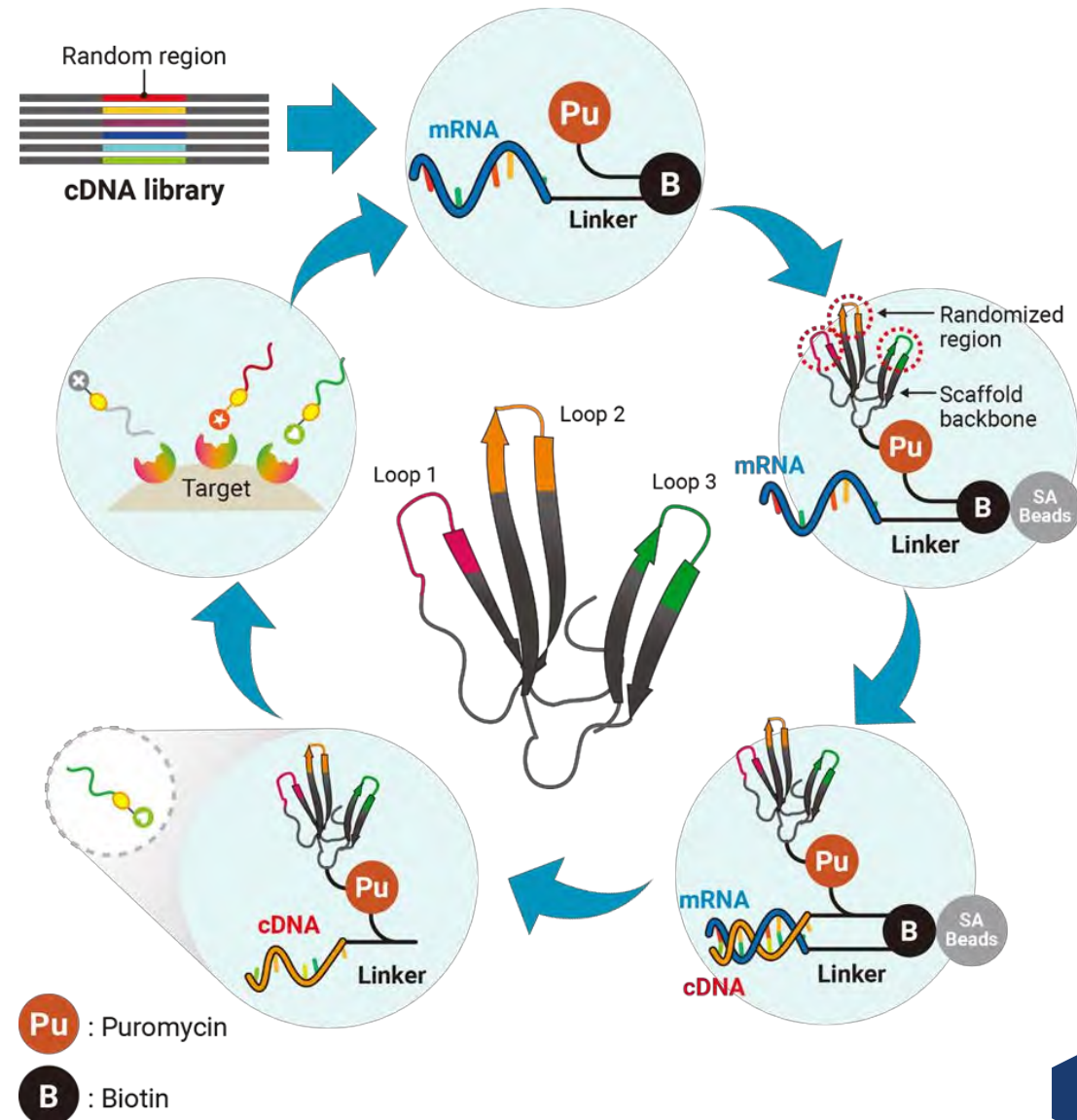
Ref.: Tai Kubo et. al., *ACS Comb. Sci.* 2016, 18, 117–129

Seed compounds **against IL-6R** discovered after 10 rounds of screening:

No.	Loop 1	Loop 2	Loop 3	Function
1	SRPRLN	GLAPRAIRAQ	TPRARTG	Non-competitive
2	QLLACR	ATRHTLGHNL	ACETPAS	Competitive and non-inhibitory
3	QLLACR	ATRHTLGHNL	ELTHPVD	Competitive and inhibitory
4	APLPYT	ATRHTLGHNL	TGPGAER	Competitive and agonistic

Ref.: Tai Kubo et. al., *Mol. Brain.* 2011, doi:10.1186/1756-6606-4-2

Scaffold protein-based screening platform using cDNA display



Discovery platform: In vitro evolution

Strong leads

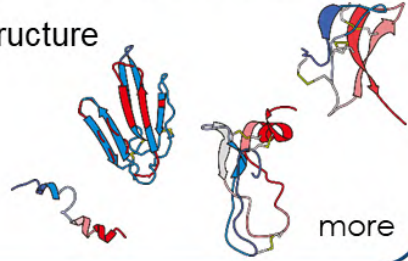
> 6 Evolutionarily optimized backbones (DRPs)

Disulfide-rich, 3D, bioactive structure

Low antigenicity

Protease resistance

Multiple functionalities



Wide target applicability

Extracellular targets: GPCRs, ion channels...

Intracellular targets

Secreted targets: Trypsin, survivin, AchBP...

Non-antigenic targets

Highly efficient screening

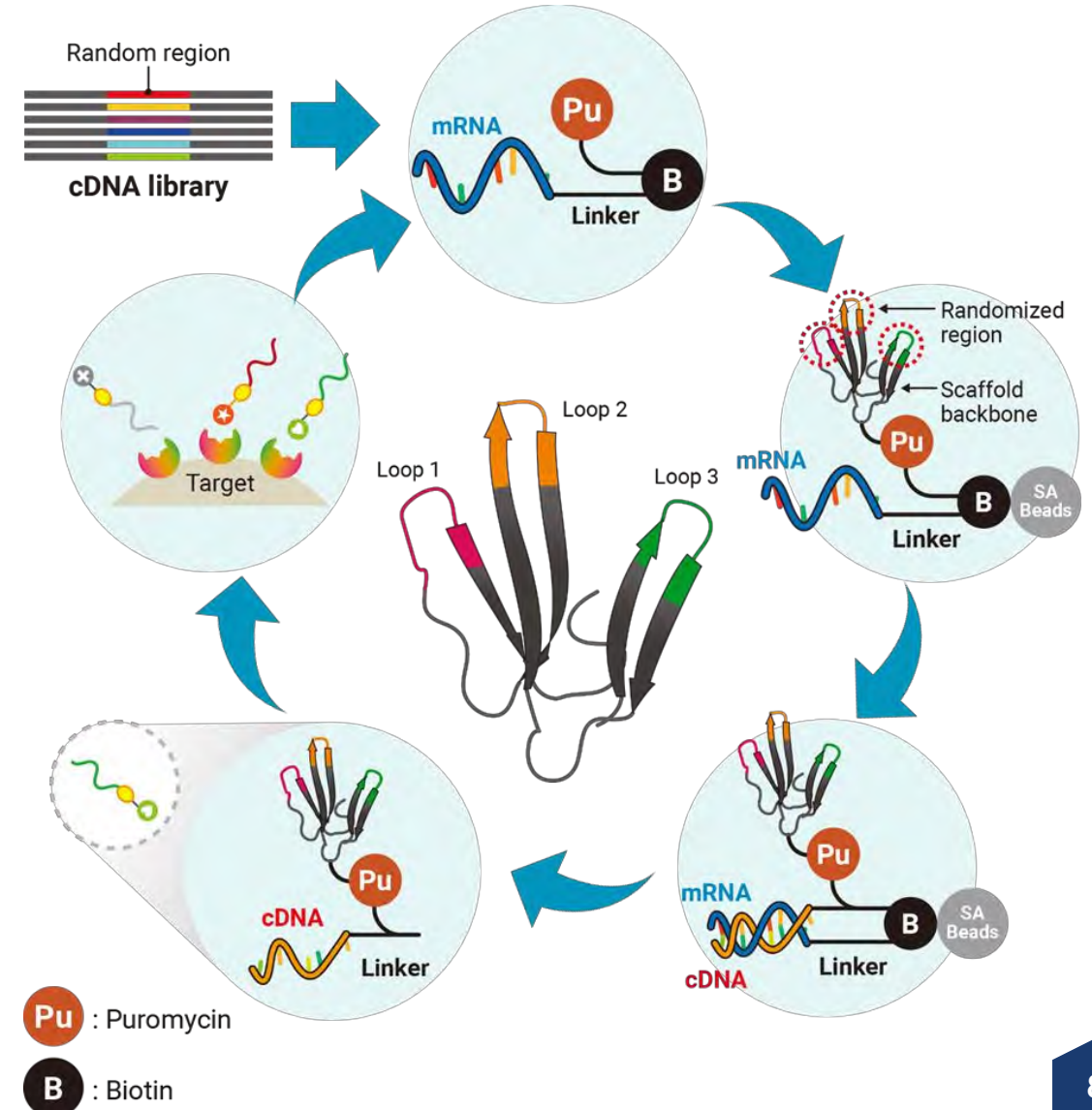
100 times larger screening space (10^{11} – 10^{13})

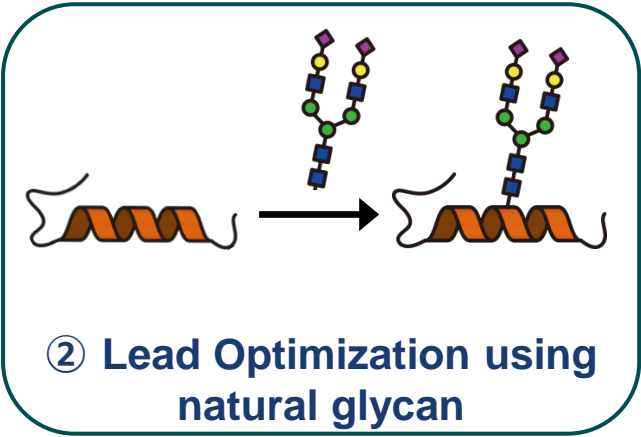
6 times faster / cycle

10 times higher final fusion yield

(Compared with traditional mRNA display systems)

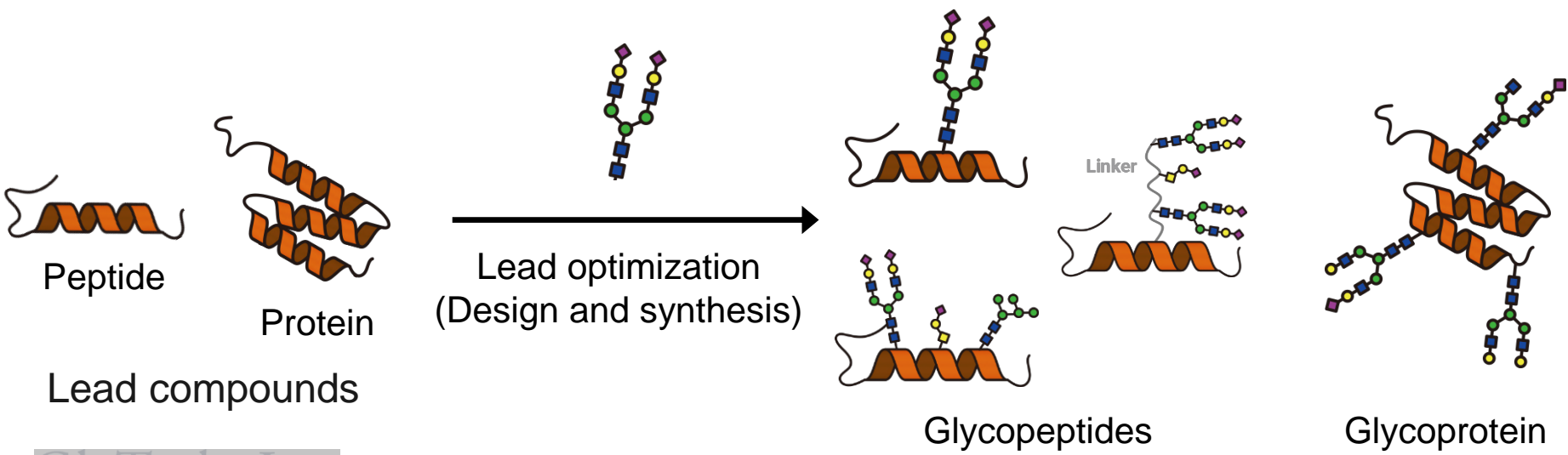
Scaffold protein-based screening platform using cDNA display





Lead Optimization using natural glycans

Controlled Glycosylation Platform

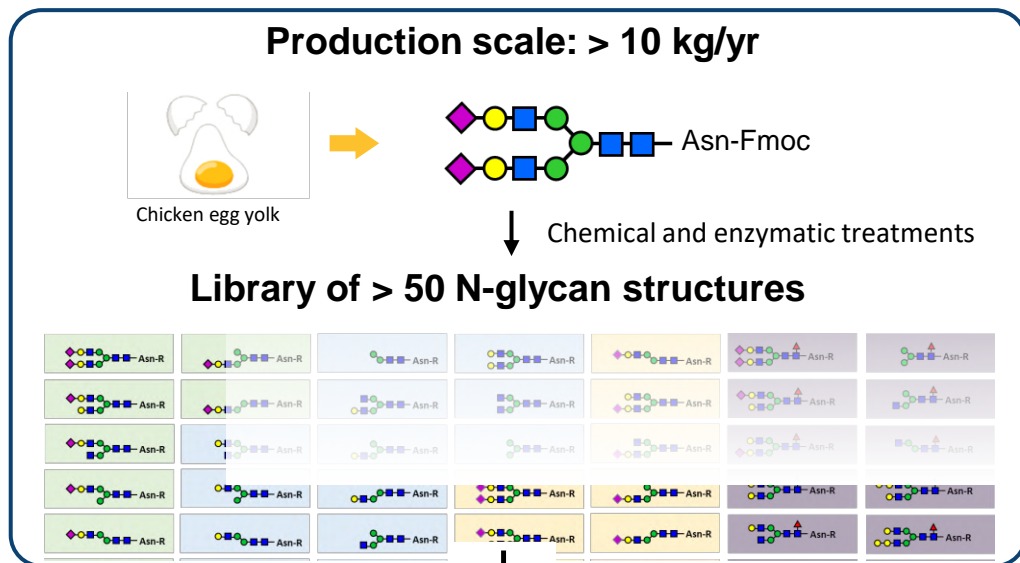


- ✓ Aqueous solubility ▲
- ✓ Circulation lifetime ▲
- ✓ In vivo biological activity ▲
- ✓ Immunogenicity ▼
- ✓ Aggregation ▼
- ✓ Drug delivery

Glycosylation revolution: Our core technology

History and Milestones

Core tech 1

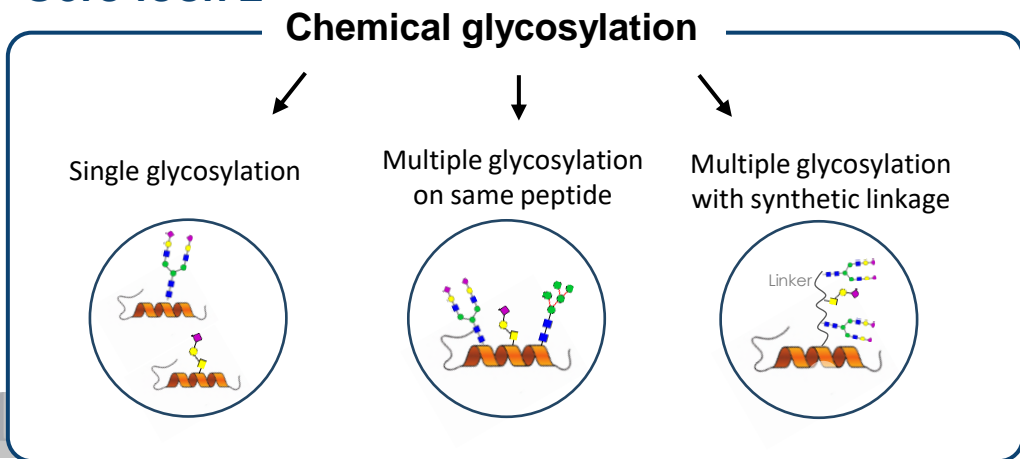


50,000,000 JPY for 100 mg
(μ g scale only available)

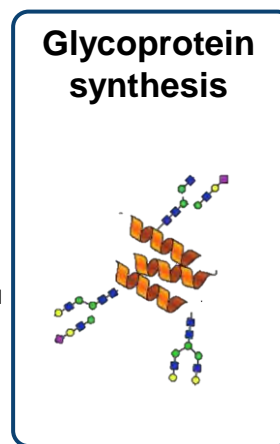
Price cut by **99%**

100,000 JPY for 100 mg

Core tech 2



Core tech 3



- 2002 Collaborative research with Prof. Yasuhiro Kajihara of Yokohama City University (currently at Osaka University)
- 2006 Initiated mass production method development
- 2009 Reached 10 kg manufacturing scale
- 2010 Animal POC proved the utility of the platform
- 2010 Initiated glycopeptide manufacturing technology
- 2011 Pilot study on cost of chemical synthesis of glycoproteins
- 2012 Published the first chemical synthesis of human interferon B in the Journal of the American Chemistry Society
- 2014 1st contract research started
- 2016 Manufactured glyco-somatostatin in GMP grade
- 2018 1st API sales start
- 2020 GlyTech's asset, glyco-somatostatin, finished Phase I clinical trial in healthy volunteers in Japan

Related research

1. Glycolibrary preparation:

Prompt Chemoenzymatic Synthesis of Diverse Complex-Type Oligosaccharides... (*Chem. Eur. J.* 2004, 10, 971)

2. Glycopeptide synthesis:

① Solid-phase synthesis of sialylglycopeptides...(*Angew. Chem. Int. Ed. Engl.* 2003, 42, 2537)

② An approach for a synthesis of asparagine-linked sialylglycopeptides... (*Chem. Eur. J.* 2007, 13, 613)

3. Glycoprotein synthesis:

① Chemical Synthesis of a Glycoprotein Having an Intact Human Complex-Type Sialyloligosaccharide (*J. Am. Chem. Soc.* 2008, 130, 501)

② Design and Synthesis of Homogeneous Erythropoietin... (*Angew. Chem. Int. Ed.*, (2009), 48, 9557)

...and so on

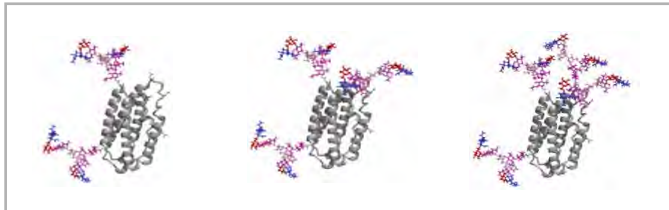
Controlled glyco-optimization

Novel modification method for biologics

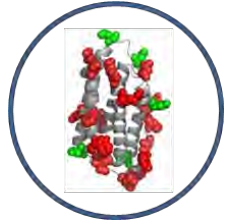
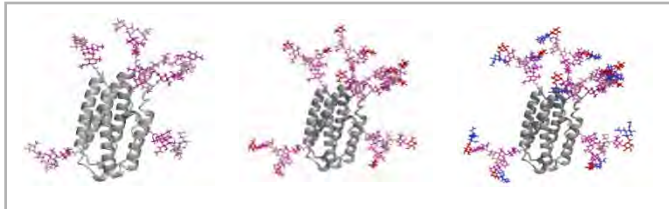
Screen for glycan position



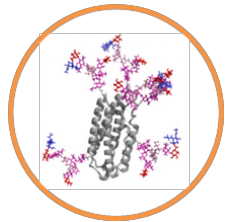
Screen for glycan number



Screen for glycan structure



Lead peptide/protein



Optimized glycoconjugate

Bio-compatible

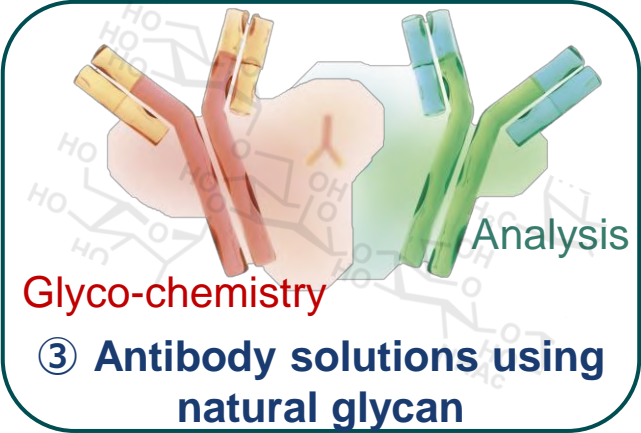
- Naturally occurring biomolecules in the human body
- Low risk of immunogenicity
- Low risk of unexpected toxicity

Site-specific modification

- **Sequence-independent design:** freely design glycosylation site, structure, and number
- **Homogeneity:** simplify purification, QC, and characterization during development

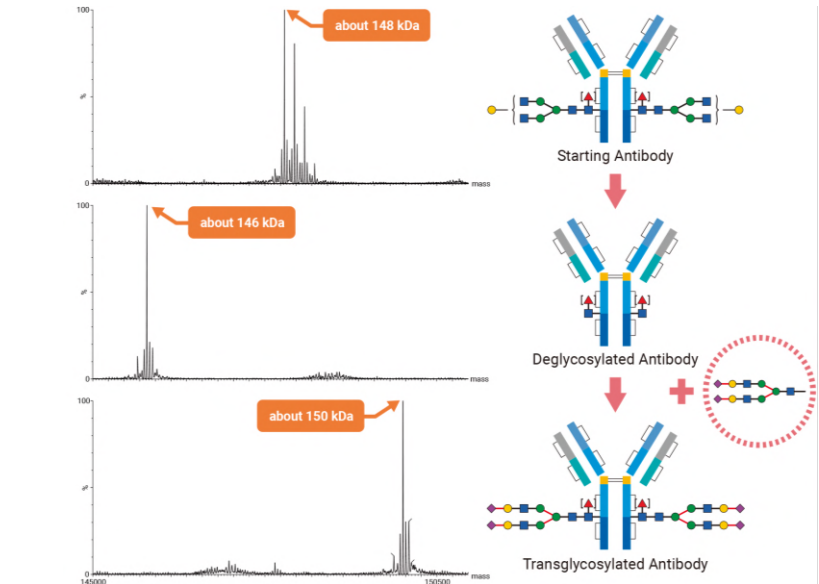
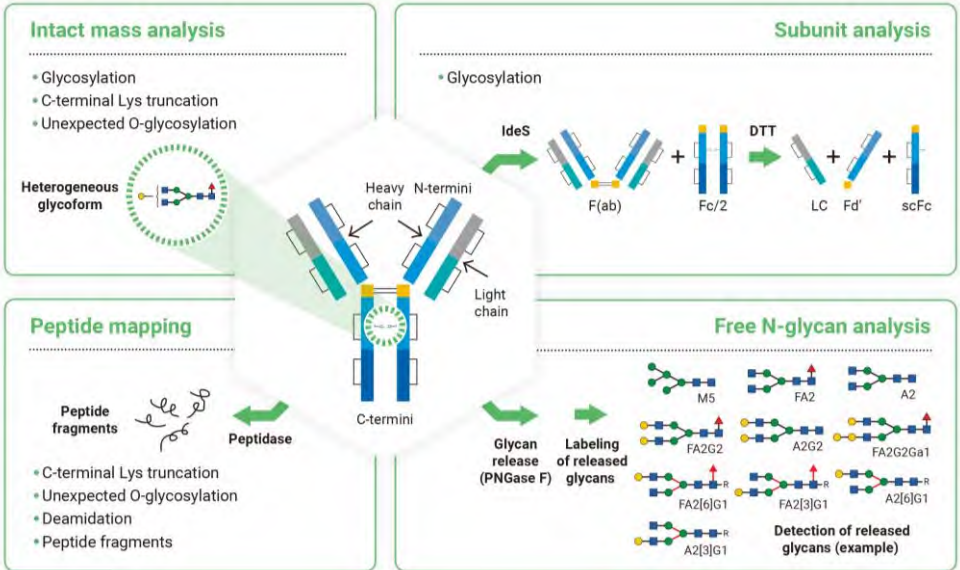
Versatile

- Wide applications from small molecules, DNA/RNA, peptides, proteins, to antibodies.
- Compatible with various conjugation chemistry
- Multiple functions:
 - ✓ Aqueous solubility ▲
 - ✓ Circulation lifetime ▲
 - ✓ In vivo biological activity ▲
 - ✓ Immunogenicity ▼
 - ✓ Aggregation ▼



Antibody solutions using natural glycan

High accuracy analysis and Glyco-chemistry Platform



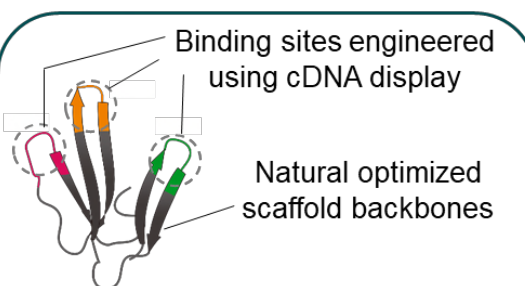
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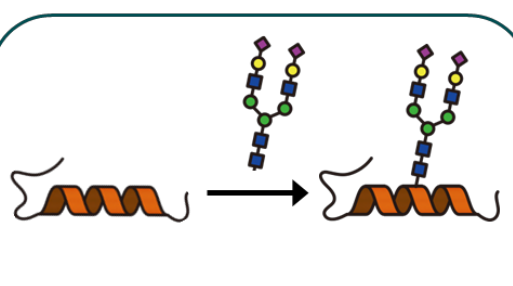
(株)糖鎖工学研究所：B-62

(株)日本触媒：R-5

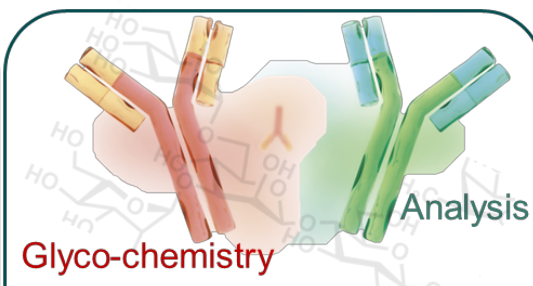
ブースにてお待ちしております。是非、お立ち寄りください
Come to our booth!



① Lead Discovery using natural scaffold



② Lead Optimization using natural glycan



③ Antibody solutions using natural glycan

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Better Health